

16073390

5.0 510(k) SUMMARY

NOV 21 2008

SUBMITTED BY:

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NAME OF DEVICE:

Trade Name:

DiaSorin LIAISON® Rubella IgG Assay
DiaSorin LIAISON® Rubella IgG Tri-Controls

Common Names/Descriptions:

Rubella IgG Test Reagents and Controls

Classification Names:

Rubella Virus Serological Reagent

Product Code:

LFX JJX

PREDICATE DEVICE:

Bayer Diagnostics, ADVIA Centaur Rubella IgG assay, K003412

DEVICE DESCRIPTION:

INTENDED USE: The LIAISON® Rubella IgG uses chemiluminescence immunoassay (CLIA) technology on the LIAISON® Analyzer for the qualitative determination of IgG antibodies to rubella virus in human serum specimens. It is intended for use as an aid in the determination of immune status to rubella in individuals including pregnant women.

The performance of this device has not been established for cord blood, neonatal samples, or for any matrices other than human serum. Likewise, performance has not been established for population(s) of immunocompromised or immunosuppressed individuals.

The LIAISON® Rubella IgG Tri-Control kit is intended for use as assayed quality control samples to monitor the performance of the LIAISON® Rubella IgG assay.

KIT DESCRIPTION:

The method for qualitative determination of specific IgG to Rubella virus is an indirect chemiluminescence immunoassay (CLIA). All assay steps (with the exception of magnetic particle resuspension) and incubations are performed by the LIAISON® Analyzer. The principal components of the test are magnetic particles (solid phase) coated with Rubella antigen and a conjugate of mouse monoclonal antibody to human IgG linked to an isoluminol derivative (isoluminol-antibody conjugate). During the first incubation, Rubella virus antibodies present in the calibrators, specimens or controls bind to the solid phase. During the second incubation, the antibody conjugate reacts with Rubella virus IgG already bound to the solid phase. After each incubation, the unbound material is removed with a wash cycle. Subsequently, the starter reagents are added and a flash chemiluminescence reaction is thus induced. The light signal,

and hence the amount of isoluminol-antibody conjugate, is measured by a photomultiplier as relative light units (RLU)

PERFORMANCE DATA:

EXPECTED VALUES

The LIAISON® Rubella IgG assay was tested with prospectively collected specimens from U.S. subjects routinely sent to the laboratory for rubella IgG testing (n=2159) and from pregnant women (n=449) to evaluate the assay's performance in these populations. Of the 2159 samples sent to the laboratory for routine rubella IgG testing, 91.7% were positive. Of the 449 pregnant women samples, 96.4% were positive. The distribution of results for IgG antibodies to rubella in these populations as determined by the LIAISON® Rubella IgG assay is summarized as follows.

Prospectively-collected Samples from Subjects sent to the Laboratory for Rubella IgG Testing:

	N	Negative	Equivocal	Positive	Prevalence
Total	2159	154	15	1990	91.7%
Gender					
Female	1848	127	14	1707	92.4%
Male	310	27	1	282	91.8%
Unknown	1	0	0	1	100%
Age (years)					
< 20	285	24	1	260	91.2%
20 – 39	1427	101	13	1313	92.0%
40 – 59	381	28	2	353	92.6%
>60	61	1	1	59	96.7%
Unknown	5	0	0	5	100%

Prospectively-collected Samples from Pregnant Women

LIAISON® Rubella IgG					
	N	Negative	Equivocal	Positive	Prevalence
Total	449	13	3	433	96.4%
Age (years)					
<20	66	2	1	63	95.4%
20 – 29	259	8	2	249	96.1%
30 – 39	117	3	0	114	97.4%
>40	6	0	0	6	100%
Unknown	1	0	0	1	100%

COMPARATIVE STUDY

A total of 2806 prospectively collected frozen specimens were tested in the study. Of these, 2608 were from non-selected subjects: 2159 subjects sent to the laboratory for routine rubella IgG testing and 449 pregnant women. Samples were divided randomly and the testing sites were blinded to samples' populations and comparator results prior to LIAISON® testing. Given the lack of statistical power to properly assess the pregnant women negative agreement an unbiased analysis of pre-selected samples was performed as shown below. Of the 2,806 specimens, 198 negative pre-selected subjects were tested: 98 subjects sent to the laboratory for routine Rubella IgG testing and 100 pregnant women tested for Rubella antibodies as part of their routine pre-natal care. The rubella antibody testing performed by the laboratories was used to define the samples as negative. No equivocal results were found in the initial predicate test of the 100 pregnant women, hence there was no need for consensus result to be performed on this cohort.

All of these specimens were tested for the presence of Rubella IgG antibodies using the LIAISON® Rubella IgG assay and a commercially available rubella chemiluminescence test kit. Three FDA cleared devices were chosen as the additional methods to test the predicate device equivocal samples. The classification of samples equivocal by the predicate device was reassigned based on the consensus of the combined 2 out of 3 results from the three ELISA results, i.e. a sample with concordant result by at least two of the three methods was defined following the consensus. If the results by the three methods were either discordant among themselves or concordant equivocal, the sample was classified as equivocal. The following tables compare the results obtained for the LIAISON® Rubella IgG assay and commercially available Rubella tests.

Specimens that were equivocal by both, the LIAISON® Rubella IgG assay and the consensus from the three ELISA tests were not included in the percent agreement calculation. Positive or negative results from the LIAISON® Rubella IgG assay were considered as non-agreements in the calculation of percent positive agreement and percent negative agreement when the corresponding comparator method result was equivocal.

Compared number of samples positive on both assays to sum of all positive samples on the reference assay + samples equivocal on the comparator method and negative on the LIAISON® Rubella IgG.

Compared number of samples negative on both assay to sum of all negative samples on the reference assay + samples equivocal on the comparator method and positive on the LIAISON® Rubella IgG.

Prospective Non-selected Subjects

LIAISON® Rubella IgG Results	Routine Samples Consensus Result ^a				Pregnant Women Samples Consensus Result ^a			
	Pos	Equiv	Neg	Total	Pos	Equiv	Neg	Total
Pos	1985	2	3	1990	416	1	2	419
Equiv	11	0	4	15	4	1	2	7
Neg	40	6	108	154	13	1	9	23
Total	2036	8	115	2159	433	3	13	449

	% Agreement	95% CI ^b	% Agreement	95% CI ^b
Positive	97.2% (1984/2042)	96.5 – 97.7%	95.8% (416/434)	93.9 – 97.3%
Negative	92.3% (108/117)	87.0 – 95.9%	64.3% (9/14) ^c	39.1 – 84.7%

^a 2 out of 3 rule using 3 additional FDA cleared assays performed on initial testing equivocal only^b Confidence Interval^c Number of samples too low to reliably calculate % negative agreement.**Pre-selected Negative Subjects**

LIAISON® Rubella IgG Results	Routine Samples Consensus Result ^a				Pregnant Women Samples			
	Pos	Equiv	Neg	Total	Pos	Equiv	Neg	Total
Pos	9	0	0	9	0	0	0	0
Equiv	0	0	0	0	0	0	0	0
Neg	3	1	85	89	1	0	99	100
Total	12	1	85	98	1	0	99	100

	% Agreement	95% CI	% Agreement	95% CI
Positive	69% (9/13)	42.8 – 88.7%	N/A	N/A
Negative	100% (85/85)	89.6 – 98.0%	100% (99/99)	97.0 – 100.0%

^a 2 out of 3 rule using 3 additional FDA cleared assays performed on initial testing equivocal only**CDC Performance Panel Results**

The following information is from a serum panel obtained from the CDC (Centers for Disease Control and Prevention) and tested on the LIAISON® Rubella IgG assay. The results are presented as a means to convey further information on the performance of this assay with a masked, characterized serum panel. This does not imply an endorsement of the assay by the CDC.

The sera panel consists of 100 specimens, 50 pairs of sera titrated by HI. There are 9 negative sera resulting in 18 negative specimens and 41 positive sera resulting in 82 positive specimens. The obtained data were submitted to the CDC for data analysis. As communicated by the CDC, the LIAISON® Rubella IgG assay resulted in 80 positive tests and 2 negative tests on the 82 positive sera, and 18 negative tests on the 18 negative sera.

CDC Biological Standard Results

The low titer (21.0 IU/mL) anti-rubella human reference serum CDC biological standard was tested neat and diluted 1:2 as described in the CLSI document I/LA6-A. The mean result of the neat standard was 3.3 Index. The mean result of the two fold diluted standard was 1.68 Index.

Precision

Assay precision performance was established at DiaSorin following protocol outlined in CLSI document, EP5-A2. A coded panel comprised of 12 frozen repository samples was prepared by DiaSorin and tested in the LIAISON® Rubella IgG assay. The panel contained samples prepared to represent negative levels, low to mid positive analyte levels and moderate to high positive levels. All panel members were divided into aliquots and stored frozen prior to testing. The coded panel was tested in four replicates per run for twenty runs. The results are summarized in the following table.

Sample ID#	N	mean (Index)	within run sd	within run %CV	between run sd	between run %CV	overall sd	overall %CV
Neg Ctl	80	<<0.1	NA	NA	NA	NA	NA	NA
Low Pos Ctl	80	1.63	0.08	5.12	0.14	8.40	0.16	9.6
Hi Pos Ctl	80	14	1.75	13.1	1.34	9.68	2.17	15.7
R01	80	0.68	0.03	4.06	0.04	5.23	0.04	6.3
R02	80	0.61	0.02	3.32	0.03	5.07	0.04	5.9
R03	80	0.90	0.03	3.64	0.04	4.74	0.05	5.9
R04	80	1.07	0.04	4.19	0.05	4.99	0.07	6.5
R05	80	0.88	0.03	3.42	0.04	5.09	0.05	6.0
R06	80	1.16	0.05	4.52	0.10	8.38	0.11	9.4
R07	80	2.4	0.11	4.85	0.21	9.13	0.23	9.9
R08	80	2.5	0.17	7.05	0.24	9.64	0.29	11.5
R09	80	3.1	0.19	6.20	0.27	8.68	0.32	10.3
R10	80	3.2	0.21	6.52	0.30	9.45	0.36	10.9
R11	80	15	1.37	9.26	1.69	11.3	2.14	13.9
R12	80	24	2.21	10.2	2.99	12.8	3.65	15.3

An assay reproducibility study was conducted at two external U.S. laboratories and at DiaSorin, according to CLSI document EP15-A2. The study included 3 different kit lots and the same coded panel as described in the twenty day study. The same coded panel was tested at all three sites, in four replicates per run for five runs. The results are summarized in the following table.

sample ID#	N	mean Index	within run SD	within run %CV	between run SD	between run %CV	between site SD	between site CV	overall sd	overall %CV
Neg Ctl	60	<<0.1	NA	NA	NA	NA	NA	NA	NA	NA
Low Pos Ctl	60	1.50	0.06	4.02	0.12	4.23	0.12	8.37	0.13	8.78
Hi Pos Ctl	60	12.6	1.0	8.17	1.30	6.04	1.28	17.0	1.64	13.09
R01	60	0.67	0.02	3.56	0.03	4.27	0.02	16.8	0.04	5.70
R02	60	0.59	0.02	3.02	0.04	4.90	0.02	12.6	0.04	6.90
R03	60	0.90	0.02	2.51	0.06	6.12	0.02	4.21	0.06	6.73
R04	60	1.06	0.04	4.15	0.09	6.37	0.05	1.12	0.10	9.07
R05	60	0.88	0.03	3.21	0.06	6.50	0.02	6.47	0.07	7.53
R06	60	1.12	0.03	2.77	0.09	6.44	0.06	6.83	0.10	8.59
R07	60	2.3	0.1	3.36	0.22	4.14	0.20	10.3	0.22	9.54
R08	60	2.4	0.1	4.03	0.26	7.52	0.17	8.02	0.27	11.07
R09	60	3.1	0.1	4.77	0.26	7.68	0.15	9.56	2.90	9.46
R10	60	3.2	0.2	5.87	0.28	7.82	0.10	8.05	0.33	10.45
R11	60	14.3	1.0	7.05	2.03	11.32	1.19	18.6	2.2	15.62
R12	60	21.7	1.4	6.56	2.24	6.79	1.95	18.8	2.66	12.25

Traceability as Compared to the international preparation RUBI-1-94 - NIBSC (WHO 1st International Standard for anti-Rubella Immunoglobulin, Human - 1997): The concordance of the assay with the WHO International Standard was evaluated using serial dilutions of the standard preparation. The dilutions were tested with two lots of in the LIAISON® Rubella IgG. The cut-off (=1 Index) calculated by interpolation on Index doses corresponds to 32400 RLUs. This RLU value calculated by interpolation on the WHO curve is 9.42 IU/mL.

dilutions	Expected index	Actual index (mean)	Expected WHO dose (IU/mL)
1:8	20.0	20.4	200
1:16	10.0	10.1	100
1:32	5.0	4.7	50
1:64	2.5	2.2	25
1:128	1.3	1.32	12.5
1:256	0.63	0.67	6.25
1:512	0.31	0.24	3.13

Linear regression between WHO doses (IU/mL) vs Index:

Linear regression	Lot 1	Lot 2
R square	0.9987	0.9982
Intercept	0.1081	0.1542
Slope	0.1086	0.0962
Result at WHO cut off	0.98 Index	0.81 Index

Cross-reactions: The cross-reactivity study for the LIAISON® Rubella IgG assay was designed to evaluate potential interference from other organisms that may cause symptoms similar to Rubella virus infection (VZV, Measles, Mumps), other organisms that may cause infectious disease (HAV, HBV, HCV, HIV, CMV, HSV, EBV, *Toxoplasma gondii*, Parvovirus, Treponema pallidum) and from other conditions that may result from atypical immune system activity (hypergammaglobulin, antinuclear autoantibodies, Rheumatoid Factor). Samples for these studies were pre-screened with another commercially available Rubella IgG assay. If found negative for Rubella IgG antibodies they were used to study potential cross-reactivity. The presence of IgG antibodies to the potential cross-reactants in the samples was confirmed using FDA-cleared assays.

Organism/condition	Number of Expected Negative Samples	LIAISON® Positive or equivocal Result
anti-HAV	59	0/59
CMV IgG	58	0/58
HBsAg	3	0/3
HSV ½ IgG	67	0/67
Toxoplasma IgG	12	0/12
VCA IgG	70	0/70
VZV IgG	50	0/50
Measles IgG	3	0/3
Mumps IgG	2	0/2
Anti-HCV	3	0/3
Anti-HIV 1/2	2	0/2
Parvovirus IgG	2	0/2
γ-globulin	3	0/3
ANA	11	0/11
RF	1	0/1
<i>Treponema pallidum</i>	1	0/1

No positive result was found for the specimens when tested by LIAISON® Rubella IgG.

WARNING: Assay Interference due to circulating HAMA has not been evaluated. The user is responsible for establishing cross-reactivity performance with these antibodies.

Potentially Interfering Substances

The DiaSorin LIAISON® Rubella IgG assay was evaluated for interference according to CLSI Document EP7. A panel of 12 samples with rubella Index values ranging from 0.61 - 19.4 were tested with two levels each of hemoglobin (500 and 1000 mg/dL), bilirubin (10 and 20 mg/dL) and triglycerides (500 and 3000 mg/dL). None of the interferents at the levels tested produced a significant change in the qualitative results of the assay.

Hook effect

No hook effect was found when two specimens with high level of anti-rubella IgG were tested. The specimens were tested neat and after serial dilution. Each point was tested in triplicate using one kit lot.

The specimens resulted in the estimated index values above the measuring range as expected for specimens with high level of anti-rubella IgG, indicating no specimen misclassification.

CONCLUSION

The submitted material in this premarket notification is complete and supports a substantial equivalence decision. The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-002

JAN 11 2013

DiaSorin, Inc.
C/O Mari Meyer
Senior Manager, Regulatory Affairs
1951 Northwestern Avenue
Stillwater, MN 55082

Re: K073390

Trade/Device Name: LIAISON® Rubella IgG
LIAISON® Rubella IgG Tri-Controls

Regulation Number: 21 CFR 866.3510

Regulation Name: Rubella Virus Serological Reagents

Regulatory Class: II

Product Code: LFX, JJX

Dated: November 10, 2008

Received: November 12, 2008

Dear Ms. Meyer:

This letter corrects our substantially equivalent letter of November 21, 2008.

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must

comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostics and Radiological Health at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to <http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm> for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address <http://www.fda.gov/cdrh/industry/support/index.html>.

Sincerely yours,

Uwe Scherf for

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of In Vitro Diagnostics and Radiological
Health
Center for Devices and Radiological Health

Indication for Use

510(k) Number (if known): K073390

Device Name: LIAISON® Rubella IgG and LIAISON® Rubella IgG Tri-Controls.

Indication For Use: The LIAISON® Rubella IgG uses chemiluminescence immunoassay (CLIA) technology on the LIAISON® Analyzer for the qualitative determination of IgG antibodies to rubella virus in human serum specimens. It is intended for use as an aid in the determination of immune status to rubella in individuals including pregnant women.

The performance of this device has not been established for cord blood, neonatal samples, or for any matrices other than human serum. Likewise, performance has not been established for population(s) of immunocompromised or immunosuppressed individuals.

The LIAISON® Rubella IgG Tri-Control kit is intended for use as assayed quality control samples to monitor the performance of the LIAISON® Rubella IgG assay.

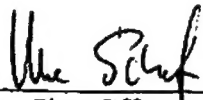
Prescription Use X
(21 CFR Part 801 Subpart D)

And/Or

Over the Counter Use
(21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)



Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K073390